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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/625,142	07/23/2003	Peter Fuenfschilling	100-8345F	8284

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CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

EXAMINER	
MCKENZIE, THOMAS C	
ART UNIT	**PAPER NUMBER**
1624	

DATE MAILED: 08/02/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/625,142	FUENFSCHILLING ET AL.	
	Examiner	Art Unit	
	Thomas McKenzie, Ph.D.	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-22* is/are pending in the application.

4a) Of the above claim(s) *14-16 and 18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-13,17 and 19-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 08/926,722.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/03,9/03/&9/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to an election filed on 5/10/05. There are twelve claims pending and eight under consideration. Claims 17 and 19-22 are compound claims. Claims 11-13 are method of making claims. The application concerns some rapamycin compounds, and ascomycin compounds and purification thereof.

2. Specifically this application concerns rapamycin or Sirolimus, Registry Number 53123-88-9, 40-O-(2-hydroxy)ethyl rapamycin or Everolimus, registry Number 159351-69-6, ascomycin, Registry Number 104987-12-4, 33-epi-chloro-33-desoxyascomycin or Pimecrolimus, Registry Number 137071-32-0, and FK506 or Tacrolimus, Registry Number 104987-11-3. Since all five have registry Numbers they are known compounds and rapamycin, 40-O-(2-hydroxy)ethyl rapamycin, 33-epi-chloro-33-desoxyascomycin, and FK506 are all articles of commerce.

3. The Examiner assumes that 40-O-(2-hydroxy)ethyl rapamycin is the substance known to Chemical Abstracts as 42-O-(2-hydroxy)ethyl rapamycin.

Election/Restrictions

4. Applicant's election without traverse of group II, claims 11-13, 17, and 19-22 in the reply filed on 5/10/05 is acknowledged.

5. Claims 14-16 and 18 withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable

generic or linking claim. Election was made **without** traverse in the reply filed on 5/10/05.

Information Disclosure Statement

6. The information disclosure statement filed 9/16/03 fails to comply with 37 CFR 1.98(a)(1), which requires the following: (1) a list of all patents, publications, applications, or other information submitted for consideration by the Office; (2) U.S. patents and U.S. patent application publications listed in a section separately from citations of other documents; (3) the application number of the application in which the information disclosure statement is being submitted on each page of the list; (4) a column that provides a blank space next to each document to be considered, for the examiner's initials; and (5) a heading that clearly indicates that the list is an information disclosure statement. The information disclosure statement has been placed in the application file, but the information referred to therein has not been considered. If an IDS listing includes a copy of an initialed IDS listing from another application, the IDS listing does not comply with the requirements under 37 CFR 1.98(a)(1).

Claim Objections

7. Objection is made to claims 21 and 22 under 37 CFR 1.75 as being substantial duplicates of claims 19 and 20. When two claims in an application are duplicates or else are so close in content that they both cover the same thing,

despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). If claim 21 should depend upon claim 14, then these are identical claims. The issue of the claim dependency is discussed below.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11-13, 19, and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "a rapamycin or an ascomycin" is indefinite for two reasons. From the use of the articles "a" and "an" it would appear that Applicants are intending to claim two genera of compounds but it is unclear are the members of these two genera. Firstly, both rapamycin and ascomycin are specific compounds. How do the genera differ from these compounds? The fourth paragraph on page 3 merely lists these five compounds but does not describe the families. Secondly, how can FK506 be an ascomycin? FK506 has a trans double bond in the macrolactone skeleton and ascomycin has a cis double bond at the same position. The Examiner suggests naming the species that Applicants are claiming.

9. Claims 17, 20, and 22 recites the limitation "FK506" in the last line of each claim. There no antecedent basis for this limitation in the parent claims 11, 19, and 21, which recite the limitation "an ascomycin" for the reason cited above.

10. Claims 21 and 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims depend ultimately upon non-elected claim 14, which is drawn to cyclosporin alone. Should claim 21 depend upon claim 19 instead?

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 11, 19, and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Hauske ('060). The compound FK520 differs from FK506 by the replacement of the allyl group adjacent to the ketone function in the macrocycle by an ethyl group. As such it would be an ascomycin under Applicants lose definition. Purification by counter current distribution using 10:1 heptane:acetronitrile solvent system is

taught in lines 54-59, column 9. Identification of the active compound as FK520 is taught in lines 40-43, column 10. Thus, the present claims 19 and 21 are taught.

12. Claims 19-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Gletsos (EP 652,219 A1). This reference teaches the purification of both Rapamycin and FK506 by extraction. Such a teaching is found in Examples 1-9, spanning line 29, page 6 through line 34, page 8. Applicants claim the compounds made by the process of counter-current extraction. However, the MPEP §2113 states, "even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted) (claim was directed to a novolac color developer. The process of making the developer was allowed. The difference between the inventive process and the prior art was the addition of metal oxide and carboxylic acid as separate ingredients instead of adding the more expensive pre-reacted metal carboxylate. The product-by-process claim was rejected because the end product, in both the prior art and the allowed process, ends up containing metal

carboxylate. The fact that the metal carboxylate is not directly added, but is instead produced in-situ does not change the end product.)."

13. Claims 19-22 are rejected under 35 U.S.C. 102(e) as being anticipated by Chu ('595). This reference teaches the purification of Rapamycin, Tacrolimus, and Ascomycin by membrane filtration. This teaching is found in lines 34-35, column 3.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

14. Claims 19-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Baumann (EP 427680 A1). This reference teaches the purification of Pimecrolimus by silica gel chromatography. Such a teaching is found in Example 66a, page 29.

15. Claims 19-22 are rejected under 35 U.S.C. 102(e) as being anticipated by Cottens ('772). This reference teaches the purification of Everolimus by silica gel chromatography. This teaching is found in Example 8, lines 53-67, column 12.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Double Patenting

16. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969). A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used

to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b). Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 19 and 21 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 6,706,727. Although the conflicting claims are not identical, they are not patentably distinct from each other because U.S. Patent No. 6,706,727 claims various ethyl ascomycin compounds prepared by counter current extraction. The present application claims ascomycin generally.

Allowable Subject Matter

17. Claims 12, 13, and 17 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, 2nd paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims. The following is a statement of reasons for the indication of allowable subject matter: Applicants process claims are patentable over Wang-Fan (Journal of Chromatography, A), which teaches purification of by Quattro counter-current chromatograph. However the 1999 publication date of this reference makes this an incompetent reference against Applicants claims.

Conclusion

18. Information regarding the status of an application should be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free). Please direct general inquiries to the receptionist whose telephone number is (703) 308-1235.

19. Please direct any inquiry concerning this communication or earlier communications from the Examiner to Thomas McKenzie, Ph.D. whose telephone number is (571) 272-0670. The FAX number for amendments is (571) 273-8300. The PTO presently encourages all applicants to communicate by FAX. The Examiner is available from 9:00am to 5:30pm, Monday through Friday. If attempts to reach the Examiner by telephone are unsuccessful, please contact James O. Wilson, acting SPE of Art Unit 1624, at (571)-272-0661.

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TCMcK/me